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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,539	10/04/2006	Rouli Zhou	062331-5002	8365

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
11/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,539	ZHOU ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7-11,14 and 17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12,13,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/24/05, 8/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I, claims 1-6, 12, 13, 15, and 16, in the reply filed on September 13, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 7-11, 14, and 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 13, 2007.

3. Claims 1-6, 12, 13, 15, and 16 are under examination.

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: the priority documents have been published in a language other than English and were not submitted with a certified English translation. A certified English translation is necessary to receive benefit of the earlier filing date.

Therefore, the claims receive the date of October 4, 2006 for art rejection purposes in this Office Action.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on June 24, 2005 and August 10, 2006 have been fully considered by the examiner and an initialed copy of the IDS is included with the mailing of this Office Action.

Specification

6. The disclosure is objected to because of the following informalities:

a.) In the brief description of the figures a description of the parts (i.e., A, B, C, etc.) of Figures 9, 11, 13 and 17 has not been included.

b.) The specification contains primer sequences, for example on pages 14 and 20 that are not identified by a SEQ ID No. It is not clear if these primers are listed in the sequence listing. The sequences need to be included in the sequence listing and identified by SEQ ID No.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-6, 12, 13, 15, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a.) Claims 1-6, 12, 13, 15, and 16 are vague and indefinite for reciting the phrase "cancer-related gene" in claim 1. According to Genes IV (Lewin et al, Oxford University Press, page 810, 1990), a gene is defined as "the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding regions (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons)." From the teachings of the specification, however, the nucleic acid sequences in claim 1 appear limited to the specific coding regions, and do not include expression control elements that fall under the definition of a gene. Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

b.) Claim 6 recites the limitation "said cancers" in line 2. There is insufficient antecedent basis for this limitation in the claim.

c.) Claim 6 is vague and indefinite for reciting the phrase "some epithelium sourced cancers". It is not clear which cancer types are included in some epithelium sourced cancers.

d.) Claims 15 and 16 are vague and indefinite for reciting the promoter of the human-cancer related gene LAPTM4B in claim 15. It is not clear what the promoter consists of. How much sequence does the promoter encompass? Is the promoter the core promoter elements or does it include upstream and/or downstream elements such as enhancers or insulators? While claim 16 further defines the promoter as containing SEQ ID No. 8, the term contains defines the promoter as including sequence and elements other than that of SEQ ID No. 8.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-6, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a human cancer-related gene having above 90% identity with SEQ ID Nos. 1, 2, 3, or 6. While the nucleic acid sequence of SEQ ID Nos. 1, 2, 3, and 6 are adequately described in the specification as-filed, thereby providing an adequate basis for the sequences of SEQ ID Nos. 1, 2, 3, and 6; there is insufficient written description as to the identity of a gene having above 90% sequence identity to SEQ ID Nos. 1, 2, 3, or 6 that would still maintain the function of the polypeptide.

Consequently, the specification does not provide an adequate written description of a cancer-related gene having above 90% sequence identity to SEQ ID Nos. 1, 2, 3, or 6.

The specification as filed does not provide adequate written description support for a gene having above 90% sequence identity to SEQ ID Nos. 1, 2, 3, or 6. Polynucleotides having diverse functions are encompassed by the phrase above 90% identity. Thus a broad genus having potentially highly diverse functions is encompassed by the phrase above 90% sequence identity and conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example, Skolnick et al. (Trends in Biotechnology, 2000. Vol. 18 pages 34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., Abstract and Sequence-based approaches to function prediction, page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular Abstract and Box 2). Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only SEQ ID Nos. 1, 2, 3, and 6 meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that applicant must convey with reasonable clarity to those skilled in the art that,

as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed. (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. Claims 1-6, 12, 13, 15, and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a human cancer-related gene LAPTM4B comprising the nucleic acid sequence of SEQ ID No. 1, 2, 3, or 6 or the polynucleotide which encodes SEQ ID Nos. 4, 5, or 7, does not reasonably provide enablement for DNA sequences having above 90% homology to the sequences of SEQ ID Nos. 1, 2, 3, or 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to a human cancer related gene LAPTM4B comprising DNA sequences having above 90% homology to the DNA sequences defined by SEQ ID Nos. 1, 2, 3, or 6 and capable of encoding proteins with the same or similar functions.

The specification discloses the sequences of SEQ ID Nos. 1, 2, 3, and 6. The specification does not disclose sequences having above 90% homology to SEQ ID Nos. 1, 2, 3, and 6 that have the same or similar functions.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology, 1990. Vol. 111, pages 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology, 1988. Vol. 8, pages 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of

nature human insulin (Schwartz et al, Proc Natl Acad Sci, 1987. Vol. 84, pages 6408-6411). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin, et al. Biochemistry, 1975. Vol. 14, pages 1559-1563).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Even if one has the correct amino acid sequence, a skilled practitioner would not be able to predict the level of expression of the resulting synthetic DNA sequence. Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. The results of the construction of synthetic proteins remain very unpredictable as Burgess et al, Lazar et al, Schwartz et al, and Lin et al conclusively demonstrate.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 101

12. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 1-6, 12, 13, 15, and 16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-6, 12, 13, 15, and 16, as written, do not sufficiently distinguish over genes as they exist naturally because claims 1-6, 12, 13, 15 or 16 do not particularly point out any non-naturally occurring differences between the claimed gene and the structure of naturally occurring genes.

In the absence of the hand of man, the naturally occurring genes are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" polynucleotide or polypeptide or similar language would obviate this rejection.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1, 2, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Shao, et al. (Genbank accession number AAP14034, submitted August 11, 2003) as evidenced by the specification.

The claims recite a human cancer-related gene LAPTM4B, comprising one of the following nucleotide sequences: 1) SEQ ID No: 1, SEQ ID No: 2, SEQ ID No: 3, or SEQ ID No: 6 in the sequence listings; 2) Polynucleotide that encodes SEQ ID No: 4, SEQ ID No: 5, or SEQ ID No: 7 protein sequences in the sequence listings; and 3) DNA sequences having above 90% homology to the DNA sequences defined by SEQ ID No: 1, SEQ ID No: 2, SEQ ID No: 3, or SEQ ID No: 6 in the sequence listings, and capable of encoding proteins with the same or similar functions, wherein the said gene is SEQ ID No: 1 in the sequence listings, wherein the said cancers are liver cancer and some epithelium sourced cancers.

Shao, et al. teach the amino acid sequence of SEQ ID No. 4 (see sequence alignment) upregulated in hepatocellular carcinoma. The specification discloses that the amino acid sequence of SEQ ID No. 4 is encoded by SEQ ID No. 1 (page 3 lines 17-18). Since the amino acid sequence of Shao is identical to SEQ ID No. 4 and SEQ ID No. 4 is encoded by SEQ ID No. 1, all the limitations of the claims have been met.

16. Claims 1, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Shao and Zhou (Genbank Accession number AAO84265, submitted April 21, 2003) as evidenced by the specification.

The claims recite a human cancer-related gene LAPTM4B, comprising one of the following nucleotide sequences: 1) SEQ ID No: 1, SEQ ID No: 2, SEQ ID No: 3, or SEQ ID No: 6 in the sequence listings; 2) Polynucleotide that encodes SEQ ID No: 4, SEQ ID No: 5, or SEQ ID No: 7 protein sequences in the sequence listings; and 3) DNA sequences having above 90% homology to the DNA sequences defined by SEQ ID No: 1, SEQ ID No: 2, SEQ ID No: 3, or SEQ ID No: 6 in the sequence listings, and capable of encoding proteins with the same or similar functions, wherein the said gene is SEQ ID No: 6 in the sequence listings.

Shao and Zhou teach the amino acid sequence of SEQ ID No. 7 (see sequence alignment). The specification discloses that the amino acid sequence of SEQ ID No. 7 is encoded by SEQ ID No. 6 (page 8 lines 24-25). Since the amino acid sequence of Shao and Zhou is identical to SEQ ID No. 7 and SEQ ID No. 7 is encoded by SEQ ID No. 6, all the limitations of the claims have been met.

17. Claims 1, 6, 12, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kato, et al. (WO/2000/05367, published February 3, 2000).

Claims 1 and 6 have been described supra. Claims 12 and 13 recite the expression vectors of the gene according to claim 1 and the transfected and mutated cell lines of the gene according to claim 1.

Kato, et al. teach an amino acid sequence identical to SEQ ID No. 5 (see sequence alignment). Kato, et al. teach the sequence isolated from stomach cancer cells and expressed in clone HP02419 (page 14). Kato, et al. also teach the

transfection of eukaryotic cells to express the protein. Since the protein of Kato, et al. is identical to SEQ ID No. 5, and due to the indefiniteness of "some epithelium sourced cancers" (see 112, 2nd paragraph, above), all the limitations of the claims have been met.

18. Claims 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Shao, et al. (Genbank Accession number AY198226, submitted August 11, 2003).

The claims recite the promoter of the human cancer-related gene LAPTM4B, wherein the said promoter contains a nucleotide sequence of SEQ ID No: 8.

Shao, et al. teach the nucleic acid sequence of SEQ ID No. 8 (see sequence alignment) as the promoter region of LAPTM4B. Since the sequence of Shao, et al. is identical to the instant SEQ ID No. 8, all the limitations of the claims have been met.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

November 6, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER